

## **REMARKS**

### **The Interview**

Applicant thanks the Examiner, Mr. Martin, for the courtesies extended in the course of an interview conducted at the United States Patent and Trademark Office on February 2, 2009. The present supplemental amendment is being submitted pursuant to the interview.

### **The Rejections under 35 U.S.C. §112**

Applicant respectfully submits that in view of the discussions conducted at the interview, and the present amendment to the claims, all rejections under 35 U.S.C. §112, second paragraph, are overcome. By the present amendment, Applicant has removed ambiguity by deleting the redundant language regarding transport of metabolite through the diffusion barrier. Applicant concurs with the Examiner's understanding of the specification with regard to the passage of metabolites through the diffusion barrier as meaning the same thing as passage of metabolites through at least one opening in the diffusion barrier. Applicant has also corrected a typographical error wherein "compartment" was inadvertently written as "component".

### **The Prior Art Based Rejections**

Applicant has amended the claims to make clear that in the present invention the medium within the component is stagnant so that the medium cannot mix by turbulent flow and so that transport of metabolite to a metabolizing particle in the compartment occurs only through diffusion. As Applicant's attorney explained at the interview, this language very clearly differentiates over the invention described in the Miltenburger patent.

At the interview, Applicant's attorney also explained why the size limitation of the transverse dimension of the compartment being less than 1.5 millimeter distinguishes over both the Miltenburger and Wodnicka references.

Applicant's attorney further discussed the structure of the Wodnicka system wherein an oxygen-responsive fluorescent dye is disposed in a body of silicone material which in turn is disposed on the bottom surface of a microplate well. A cell culture is placed in the well, atop the silicone body. Oxygen diffuses through the culture medium in the well to the dye in the silicone body, and the fluorescence of this dye is measured. As Applicant's attorney explained, the Wodnicka system does not have a diffusion barrier which is arranged around the metabolizing particle. Likewise Wodnicka does not show any system in which oxygen or some other metabolite diffuses through a barrier to a metabolizing particle. As Applicant's attorney explained at the interview, these features still further differentiate the present invention over Wodnicka.

**The Prior Art References of Houghton et al. and Trimarchi et al.**

At the interview, the Examiner drew Applicant's attorney's attention to a publication of Houghton et al. "Oxygen Consumption and Energy Metabolism of the Early Mouse Embryo", *Molecular Reproduction and Development* 44:476-485 (1996); and Trimarchi et al. "Oxidative Phosphorylation-Dependent and -Independent Oxygen Consumption by Individual Preimplantation Mouse Embryos", *Biology of Reproduction* 62, 1866-1874 (2000). The Examiner asked Applicant's attorney to consider these references with regard to the patentability of the herein amended claims. Applicant thanks the Examiner for the opportunity to review and comment on these references.

Applicant notes for the record that these two references were previously made of record and individually asserted against the novelty of the then-pending claims in an Office Action mailed November 2, 2007. In response thereto, Applicant, on May 1, 2008, filed an amendment and remarks addressing the references. In an Office Action mailed July 15, 2008, the Examiner acknowledged Applicant's amendment and discussion of the Houghton and Trimarchi

publications and withdrew the rejections. Applicant respectfully submits that the presently amended claims include all of the limitations of the claims at issue in the July 15, 2008 Office Action, and Applicant respectfully submits that the present claims are allowable thereover.

With regard to the Houghton reference: Disclosed is an experimental procedure in which a medium comprising metabolizing particles is positioned inside a PCR micropipette together with an oxygen saturated solution of pyrene in paraffin oil. Pyrene is a luminophore whose fluorescence is quenched by oxygen. The device is then sealed at both ends. Due to the metabolism of the metabolizing particle and the seals, an oxygen concentration gradient is established (page 478, left column, lines 3-5). However, since the micropipette is sealed in an airtight manner, Houghton et al. does not disclose a device wherein metabolite transport through a diffusion barrier is allowed by diffusion. The independent claims and all claims dependent therefrom (specifically including claims 13 and 21) are hence novel in view of Houghton et al. To the extent that the oxygen saturated paraffin oil could be considered to be a diffusion barrier, it must be emphasized that the diffusion barrier according to claim 1 is arranged around the particle, which is certainly not the case with the paraffin oil positioned as shown in Figure 1 of Houghton et al.

Regarding Trimarchi et al.: Trimarchi et al. describes a method in which a metabolizing particle is arranged in an open Petri dish and the oxygen gradient there around is measured using an oxygen-sensitive electrode. However, Trimarchi et al. does not disclose a method wherein a diffusion gradient is established throughout the medium in the compartment. As described in the discussion (page 1872, left column, lines 19-22), the oxygen concentration is only influenced some 50 micrometers away from the metabolizing particle, and due to the fact that several metabolizing particles are positioned in the Petri dish, having different metabolizing capacity,

whereby each particle establishes its own local diffusion gradient, one oxygen diffusion gradient cannot be established throughout the medium.

Furthermore, the transverse dimension of a Petri dish is several fold larger than the upper limit given in claim 1. The reference does not disclose the diameter of the selected MatTek Petri dish, but the website of MatTek Corp. discusses what they denote as standard size 35 and 50 mm disposable plastic Petri dishes. In this regard see the website <http://www.glass-bottom-dishes.com/>.

Applicant respectfully submits that in view of the previous and present amendments, and in view of the remarks and discussion presented herein, the claims at issue are patentable over the Trimarchi and Houghton references.

#### Conclusion

Applicant respectfully requests that the Examiner consider the amendment and remarks made herein and withdraw the presently pending rejections.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 07-1180.

Dated:

Respectfully submitted,

By

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